Journal of Forensic and Legal Medicine 16 (2009) 357–361

Contents lists available at ScienceDirect

Journal of Forensic and Legal Medicine

journal homepage: www.elsevier.com/jflm

Case Report

Autopsy findings in a case of tuberous sclerosis

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ARTICLE INFO

Article history:
Received 9 January 2008
Accepted 16 January 2009
Available online 25 February 2009

Keywords:
Tuberous sclerosis
Seizure
Angiofibroma
Lipomata

ABSTRACT

Tuberous sclerosis is a neurocutaneous disorder with autosomal dominant inheritance. It is characterized by the triad of seizures, mental retardation, angiofibromas of the face though the triad is not always complete. We incidentally encountered a case of tuberous sclerosis in a case of hanging. He was an epileptic. Autopsy findings included unusual findings of myocardial and renal lipomata. He also had cortical thickening of bones, cortical tubers of brain, polycystic kidney disease.

1. Introduction

Tuberous sclerosis (Bourneville's disease) is a neurocutaneous syndrome characterized by cutaneous lesions, seizures, and mental retardation.[1] It is an autosomal dominant syndrome characterized by the development of hamartomas and benign neoplasms in the brain and other tissues. Several distinct loci have been identified with indistinguishable clinical and pathological features including the TSC1 locus on 9q34 coding for hamartin and more commonly, TSC2 locus found on chromosome 16p13.3 coding for tuberin.[2] We report the autopsy findings in a case of tuberous sclerosis (TS). There are several unusual features, including myocardial and renal lipomata which are rarely reported in TS.

2. Case report

A thirty eight year old man with history of epilepsy since childhood committed suicide by hanging. The following details were given by the relatives: He was eccentric with apparently normal intelligence. His mentally retarded twin brother had died three months back due to a natural cause (reported by the relatives as cerebral hemorrhage). He was married with one daughter. He has another brother. But for the twin brothers, other members of the family were asymptomatic. He had been correctly diagnosed and managed as tuberous sclerosis. The loss of his brother might have been a stressor along with other domestic problems.

3. Autopsy findings

He was a moderately built and nourished man (165 cm height, 63 kg weight). On external examination skin showed papulonodular soft to firm swellings of various sizes distributed in various sites – in a butterfly distribution over face, neck, and trunk. Fig. 1 showing angiofibromas distributed in a butterfly pattern over nose and cheeks, Fig. 2 showing fibromas over right axilla.

He also had thick, rough hypopigmented skin patch over left lumbo sacral region of size $3 \times 3 \times 2.5$ cm with the appearance of Shagreen patch. Fig. 3 showing Shagreen patch, surrounding which macular hypopigmented skin patches are also seen.

He also had findings of lipoma behind left ear (Fig. 4), café au lait spot over right flank (Fig. 5) and hypomelanotic spots over front of legs.

The internal organs showed the following: the brain was firm to palpation with tuberous appearance. The cortex of frontal, temporal, occipital lobes were firm to palpation. The firmness was more just below the sagital sinus on either sides of the midline (Fig. 6). There were also tiny projections into the lateral ventricles (candle guttering) (Fig. 7).

The heart showed numerous fatty swellings within the myocardium (Fig. 8).

The kidneys were polycystic bilaterally with yellowish fat deposits (Fig. 9). There was increased cortical thickness of long bones (Fig. 10).

3.1. Histopathology

The following findings were the histological findings of skin from shagreen patch; there was increased collagen in dermis

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doi:10.1016/j.jflm.2009.01.015

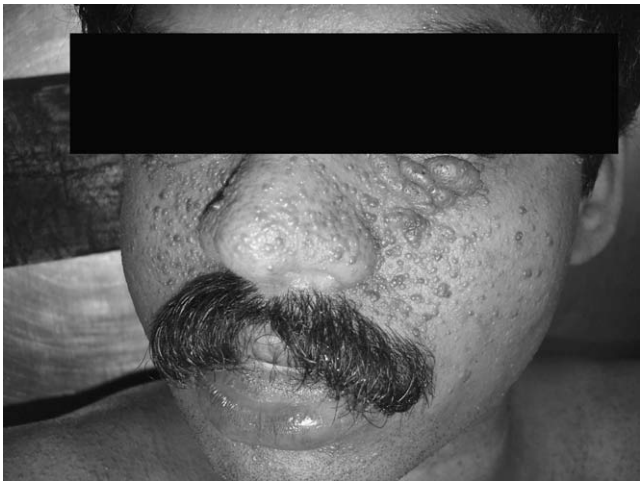

Fig. 1. 'Adenoma sebaceum' – angiofibromas of face.

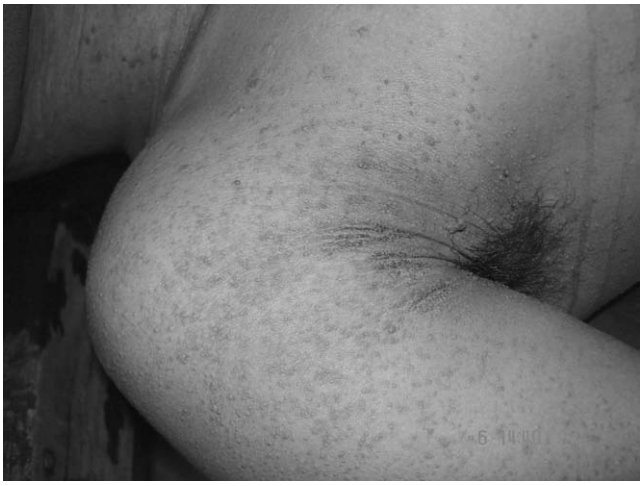

Fig. 2. Fibroma over right axilla.

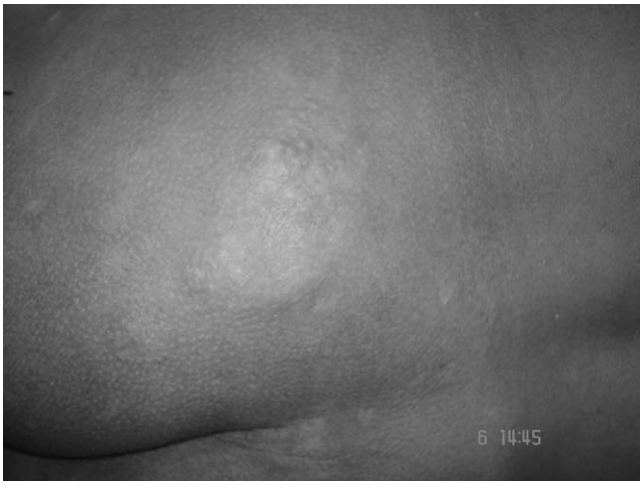

Fig. 3. Shagreen patch over left lumbosacral region.

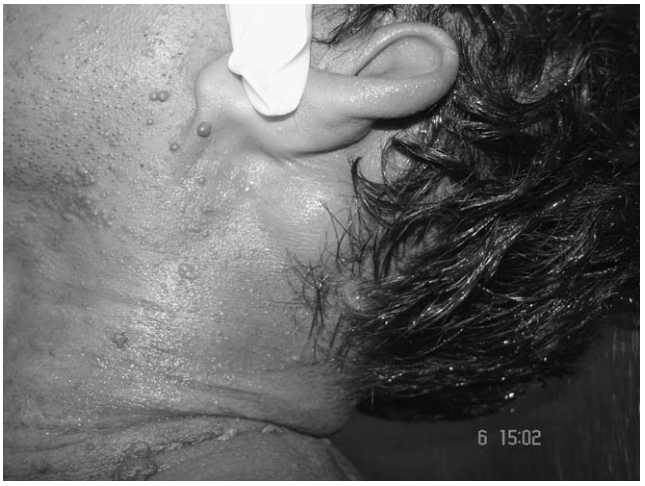

Fig. 4. Lipoma behind left ear.

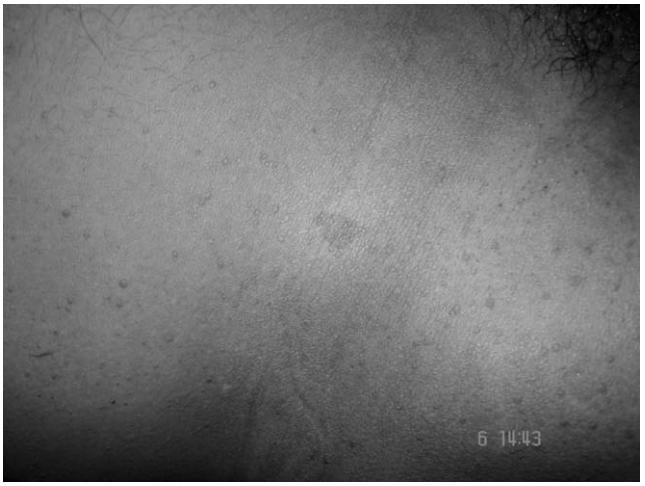

Fig. 5. Café au lait spot over right flank.

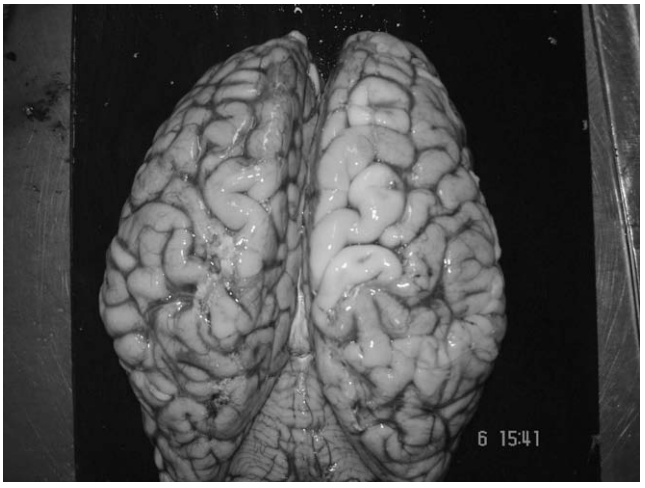

Fig. 6. Brain – cortical tubers.

(Fig. 11) and cysts (Fig. 12). The brain showed calcified nerve tissue (Fig. 13) and vessels (Fig. 14). The heart showed fat deposit between two layers of myocardium (Fig. 15) – myocardial lipomata. The kidneys showed fat deposits admist glomeruli (Fig. 16) and cysts (Fig. 17).

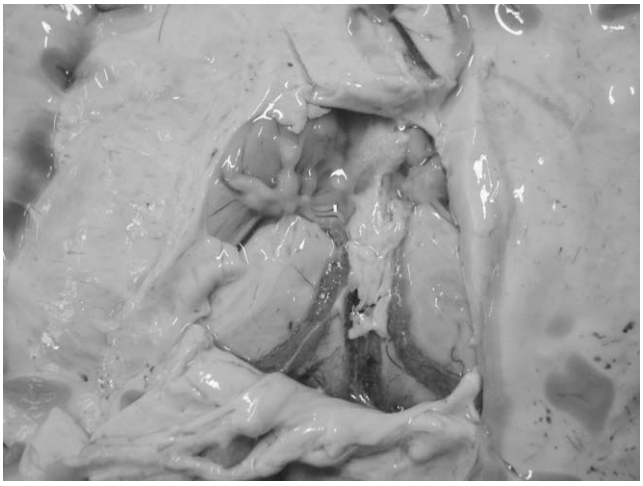

Fig. 7. Brain – candle guttering of ventricles.

Fig. 8. Heart – fatty swellings within the myocardium.

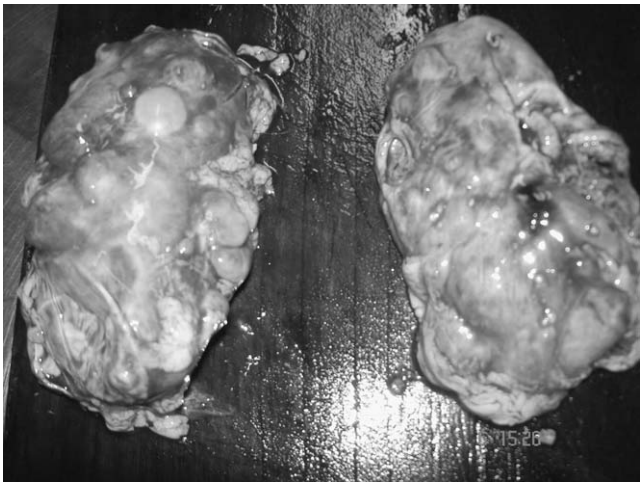

Fig. 9. Kidneys – polycystic bilaterally with yellowish fat deposits.

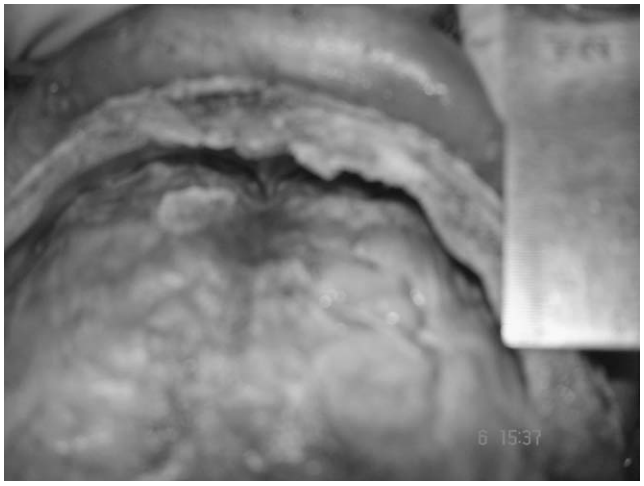

Fig. 10. Increased cortical thickness of skull.

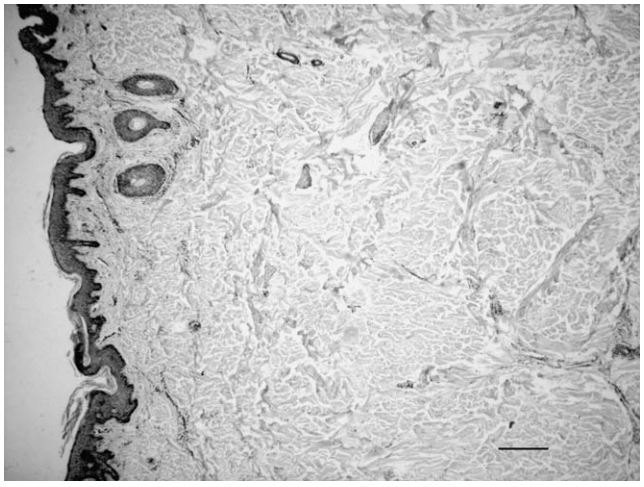

Fig. 11. Histology of a Shagreen patch showing increased collagen in the dermis.

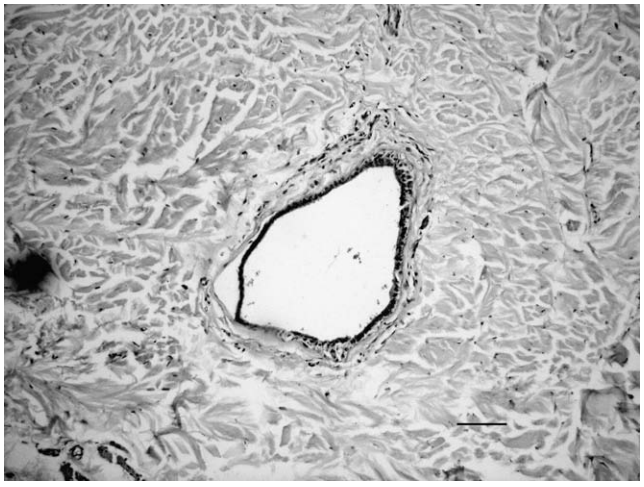

Fig. 12. Shagreen patch showing dermal cysts on histology.

4. Discussion

TS is inherited as an autosomal dominant trait, but 60–70% of cases are sporadic and are thought to represent new mutations.[3] The phenotype is highly variable. At the recent tuberous sclerosis complex consensus conference, the clinical diagnostic criteria for tuberous sclerosis complex were simplified and revised to reflect

Fig. 13. Brain histology – calcified nervous tissue.

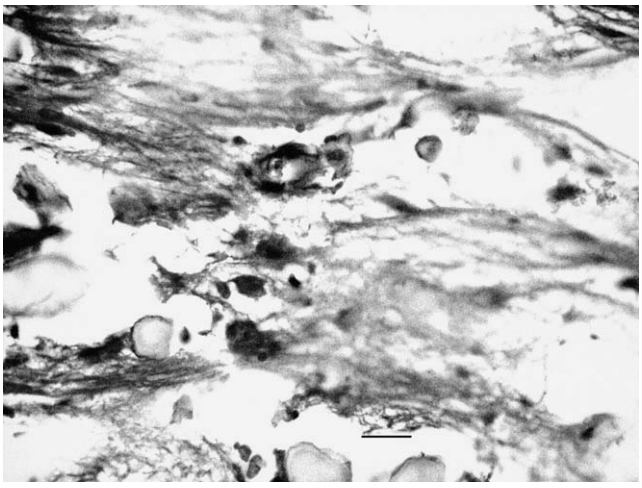

Fig. 14. Brain histology – vascular calcification.

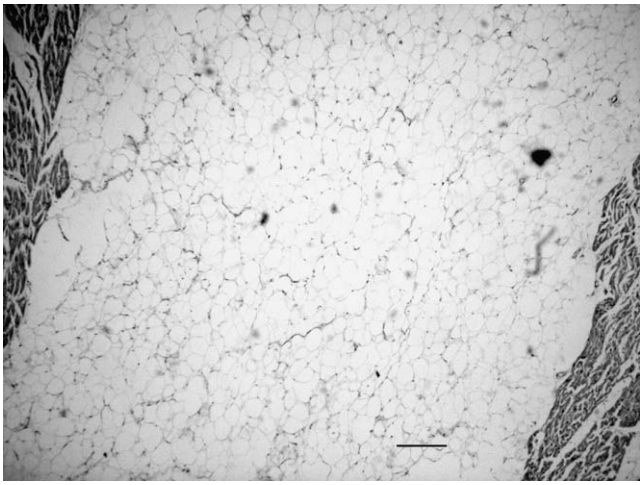

Fig. 15. Cardiac histology – myocardial lipomata.

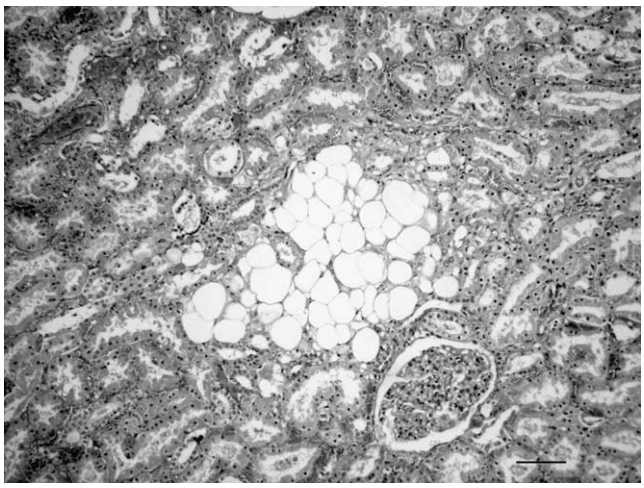

Fig. 16. Renal histology – fat deposition amidst glomeruli.

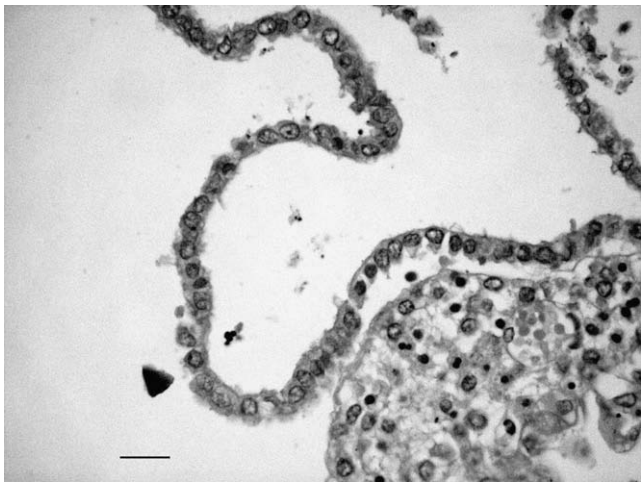

Fig. 17. Renal histology – cysts.

both new clinical information about tuberous sclerosis complex and an improved understanding of the disorder derived from molecular genetic studies. Based on this new information, some clinical signs once regarded as pathognomonic for tuberous sclerosis complex are now known to be less specific and major and minor criteria have been established.[4]

Autopsy reports of TS associated with diaphragmatic hernia[5], glomerulocystic disease, tracheo-esophageal fistula and megaureter syndrome[6], aortic aneurysms[7], dysplasia of the corpus callosum, omphalocele and malrotated colon[8] are published in literature.

In this case there are unusual findings of lipomatous hamartomas in the skin, heart, kidney and calcified atypical neurons. The abnormal neurons probably contributed to causing epilepsy in this case. Since their parents and brother are asymptomatic, the probability of spontaneous mutation stands high. His daughter, who according to the relatives is normal, is at high risk of having the disease and needs screening.

TS has an association with sudden death.[9] Fatal mechanisms in cases of tuberous sclerosis may be associated with underlying cardiovascular, renal and cerebral abnormalities. Sudden death may be due to cardiac arrhythmia, epilepsy, and intra-tumoral hemorrhage with additional complications including cardiac outflow obstruction, obstructive hydrocephalus, aneurysm rupture, and spontaneous pneumothorax. An awareness of the highly variable tissue manifestations of tuberous sclerosis and the mechanisms that may be responsible for death is necessary to establish correctly the diagnosis in occult cases (possibly with molecular confir-

mation), and to chart accurately organ changes in individuals with established disease.A case of a large epicardial lipoma associated with an unusual rupture of an infarcted interventricular septum has also been reported.[10] Spontaneous pneumothorax can be associated with tuberous sclerosis and can cause sudden death.[11]

Thus it can be concluded that there is a wide spectrum of manifestations possible in tuberous sclerosis, many of which can cause sudden death. Occult cases can be difficult to diagnose.

Conflict of Interest

None declared.

Funding

None declared.

Ethical approval

None declared.

Acknowledgement

We are thankful all staff and students of Department of Forensic Medicine for their cooperation and support and to the Department of Pathology, Government medical college, Calicut for providing the histology details and photos of slides.

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